REMARKS

Interview request

Applicants respectfully request a telephonic interview after the Examiner has reviewed the instant response and amendment. Applicants request the Examiner call Applicants' representative at (858) 720-5133.

Status of the Claims

Pending claims

Claims 1 to 30, 33 to 64, 66 to 71 and 83 to 93 will be pending and under consideration.

Claims canceled and added in the instant amendment

Claims 94 to 98 are added. Thus, after entry of the instant amendment, claims 1 to 30, 33 to 64, 66 to 71 and 83 to 98, will be pending and under consideration.

Support for the Claim Amendments

The specification sets forth an extensive description of the invention in the new and amended claims. Accordingly, no new matter has been added and the amendment can be properly entered.

The Group Restriction Requirement

The Patent Office alleged that the pending claims of the application are directed to four separate and distinct inventions (groups a through d) under 35 U.S.C. §121, as set forth on page 1 of the instant office action:

> Group I (claims 1 to 30, 33 to 64, and 66 to 71) drawn to in vitro/ex vivo methods of transducing primary cells of the hematopoietic system using a lentiviral vector and cell surface binding molecule, classified in class 435, subclass 456;
>
> Group II (claim 85) drawn to a method for the introduction of transduced cells into a living subject, classified in class 435, subclass 325;
>
> Group III (claim 86) drawn to a method of introducing a transduced cell into a tissue or organ, blastocyst, or embryonic stem cell, classified in class 435, subclass 325;

Group IV (claim 87) drawn to a method of introducing a transduced cell into a blastocyst, classified in class 435, subclass 325.

The Group Election

Applicants hereby elect Group I, claims 1 to 30, 33 to 64, and 66 to 71, including new claims 94 to 98, with traverse. Applicants' reasons for this traversal is set forth, below.

Applicants expressly reserve their right under 35 U.S.C. § 121 to file a divisional application directed to the nonelected subject matter during the pendency of this application, or an application claiming priority from this application.

The Species

The Patent Office has further alleged that the claims in Group I are directed to patentably distinct species, as set forth on pages 2 to 3 of the instant office action:

(1) The Office alleges that Applicants are required to identify and elect a single cell target (e.g., CD4+, CD8+, CD34+, dendritic cell, etc.);

(2) The Office alleges that Applicants are required to identify and elect a single cell surface binding molecule (e.g., polypeptide, a lipid, a nucleic acid, a carbohydrate, an ion, an FLT-3, a TPO, a Kit ligand, etc.);

The Species Election

In response, Applicants elect the following species, all with traverse:

(1) Regarding identification and election of a single cell target, Applicants elect CD4+ cells, with traverse.

(2) Regarding identification and election of a specific cell surface binding molecule, Applicants elect polypeptides, with traverse.

When the elected species is held to be allowable, Applicants are entitled to consideration (examination) of additional species; if all species are held to be allowable, a generic claim should be allowed (MPEP §809.02(c); pg 800-50, 8th Edition, August 2001).

Reasons to reconsider and withdraw restriction requirement

Applicants respectfully request the Patent Office reconsider and, in part, withdraw the restriction requirement for the following reasons:

Rejoining of the inventions of Groups II, III and IV to Group I

The Patent Office alleges the invention of elected Groups I, Group II, Group III and Group IV, are drawn to methods that are patentably distinct because, inter alia, each group is directed to a different method that accomplishes different scientific objectives and employs disparate methodology steps and scientific reagents (see the paragraph spanning pages 1 and 2 of the OA).

Applicants respectfully request reconsideration and rejoining of the inventions of Groups II, III and IV, including claims 85, 86 and 87, to the elected Group I.

Group I, including the three independent claims 1, 34, and 88, comprises methods for stable transduction of cells, including hematopoietic system and/or hematopoietic stem cells, comprising simultaneous contact of any member of a genus of lentiviral vectors and any member of a genus of cell surface binding molecules or molecules that physically interact with a receptor, marker, or other recognizable moiety on the surface of the primary cell or hematopoietic stem cell.

In particular, claim 1 is directed to methods for stable transduction of primary cells of the hematopoietic system and/or hematopoietic stem cells comprising contacting the surface of said primary cell or hematopoietic stem cells at the same time *in vitro* or *ex vivo* with both a lentiviral vector and at least one molecule which binds said cell surface, wherein at least about 75% of the cells are stably transduced after about seven to ten days, or at about 14 days.

Claim 34, after entry of the instant amendment, is directed tomethods for stable transduction of primary cells of the hematopoietic system and/or hematopoietic stem cells comprising (a) isolating from an individual a primary cell of the hematopoietic system and/or a hematopoietic stem cell; and (b) contacting the primary cell or hematopoietic stem cell simultaneously *in vitro* or *ex vivo* with a lentiviral vector and an at least one molecule that physically interacts with a receptor, marker, or other recognizable moiety on the surface of the primary cell or hematopoietic stem cell, wherein greater than about 75% of the primary cells or hematopoietic stem cells are stably transduced after about seven to ten days, or at about 14 days,

and optionally the cell surface binding molecule comprises a polypeptide, a lipid, a nucleic acid, a carbohydrate or an ion.

Claim 88 is directed to methods for stable transduction of a cell with a lentiviral vector comprising contacting the cell at the same time *in vitro* or *ex vivo* with a lentiviral vector and at least one cell surface binding molecule, wherein the lentiviral vector is pseudotyped, wherein the pseudotyping comprises co-transfecting or co-infecting a packaging cell with both the lentiviral vector genetic material and genetic material encoding at least one envelope protein of another virus or a cell surface molecule, wherein at least about 75% of the cells are stably transduced after about seven to ten days, or at about 14 days, and optionally at least 75% of the cells remain stably transduced after about 14 days.

Claims 85, 86 and 87, are dependent claims, and, after entry of the instant amendment, claims 85, 86 and 87, are directed to the methods of claim 1 or claim 34, further comprising: introducing the transduced cell into a living subject (claim 85); introducing the transduced cell into a tissue or an organ (claim 86); introducing the transduced cell into a blastocyst (claim 87).

One or more claims may be presented in dependent form, referring back to and further limiting another claim or claims in the same application. Claims in dependent form shall be construed to include all the limitations of the claim incorporated by reference into the dependent claim. 37 CFR §1.75. See also MPEP §608.01(i).

Accordingly, claims 85, 86 and 87, as dependent claims, incorporate all the limitations of claim 1 or claim 34, and they further limit claims 1 and 34. Thus, each of claim 85 (Group II), 86 (Group III) and 87 (Group IV), is directed to the same method that accomplishes the same scientific objective, but with a further, or additional, limitation. Claim 85, 86 and 87, only employ a methodology step or scientific reagent different from that of independent claim 1 or claim 34 in that the further (additional) limitation in the dependent claim employs additional methodology step(s) or scientific reagent(s). Thus, claim 85 (Group II), 86 (Group III) and 87 (Group IV) can be properly rejoined to Group I.

Furthermore, because claims 85, 86 and 87, are dependent claims and incorporate all the limitations of claim 1 or claim 34, and further limit claims 1 and 34, a thorough search of the invention of claim 1 or claim 34 necessarily includes the invention set forth in claims 85, 86 and 87, because the claims 85, 86 and 87, are drawn to narrower embodiments of claims 1 and 34. Thus, because a search of claim 85 (Group II), 86 (Group III) and 87 (Group IV) after a thorough search of Group I will not be an undue burden on the Office, claim 85 (Group II), 86 (Group III) and 87 (Group IV) can be properly rejoined to Group I.

The species restriction should be a species election

The Patent Office has further alleged that the claims in Group I are directed to patentably distinct species and Applicants are required to identify and elect (1) a single cell target (e.g., CD4+, CD8+, CD34+, dendritic cell, etc.); and, (2) a single cell surface binding molecule (e.g., polypeptide, a lipid, a nucleic acid, a carbohydrate, an ion, an FLT-3, a TPO, a Kit ligand, etc.).

Applicants respectfully submit that these species (target cells and cell surface binding molecules) are not proper patentably distinct restriction groups (where each group would need a separate divisional application), but rather should be an election of species under 35 U.S.C. §121, 37 CFR 141(a) ("[t]wo or more independent and distinct inventions may not be claimed in one national application, except that more than one species of an invention, not to exceed a reasonable number, may be specifically claimed in different claims in one national application, provided the application also includes an allowable claim generic to all the claimed species and all the claims to species in excess of one are written in dependent form (§ 1.75) or otherwise include all the limitations of the generic claim.") (emphasis added)

Addtionally, if the Patent Office withdraws the "patentably distinct species requirement" and instead requests an election of species under 37 CFR 141(a), and these elected species are held to be allowable, Applicants are entitled to consideration (examination) of additional species; and if all species are held to be allowable, a generic claim should be allowed (MPEP §809.02(c); pg 800-50, 8th Edition, rev. 2, May 2004).

Group I, including the three independent claims 1, 34, and 88, comprises methods for stable transduction of primary cells of the hematopoietic system and/or hematopoietic stem cells, comprising simultaneous contact (contact at the same time) of any member of a genus of lentiviral vectors and any member of a genus of cell surface binding molecules or molecules that physically interact with any cell target, including any receptor, marker, or other recognizable moiety on the surface of the primary cell of the hematopoietic system or the hematopoietic stem cell.

Thus, in making this restriction the Patent Office has erroneously incorporated into the independent claims 1, 34 and 88, the limitations of dependent claims directed to specific target cells and specific cell surface binding molecules, thereby improperly limiting what Applicants consider their invention.

For example, if the elected invention was limited only to methods directed to transducing, e.g., CD4+ cells, CD8+ cells or CD34+ cells, then the limitations of, inter alia, dependent claim 14 (herein said ... cell is a CD4 positive cell), claim 16 (wherein the ... cell is a CD4 or CD8 positive cell), claim 17 (wherein said ... cell is a CD34 positive cell) would be improperly incorporated into the independent claims.

Likewise, if the elected invention is limited to single cell surface binding molecule, the elected methods would be improperly limited, e.g., to only one of the embodiments of claim 18, claim 19 (wherein said at least one cell surface binding molecule comprises ... FLT-3 ligand, TPO ligand and Kit ligand or polypeptides ...), claim 21 (... CD34, CD3, CD28, GM-CSF, IL-4, TNF-alpha; GM-CSF, interferon-alpha; and antibodies ...), claim 22 (... CD3 antibodies and cell surface binding fragments thereof, CD28 antibodies and cell surface binding fragments ...), claim 23 (...a combination of CD3 and CD28 antibodies immobilized ...), or to one of the embodiments of any of new claims 94 to 96 (... wherein the at least one cell surface binding molecule comprises a polypeptide, a lipid, a nucleic acid, a carbohydrate or an ion).

For example, if the elected invention is limited to methods using a single cell target cell, e.g., the elected $CD4^+$ cells, then the limitations of, inter alia, dependent claim (wherein said primary hematopoietic cell is a CD4 positive cell or is a hematopoietic stem cell of a CD4 positive cell) is

improperly incorporated into the independent claims. Likewise, if the elected invention is limited to methods using a single cell target cell, the genus of cells transduced by the elected methods would be improperly limited, e.g., the embodiments of claim 15 (wherein said primary cell of the hematopoietic system or hematopoietic stem cell is a lymphocyte or a precursor thereof) or claim 17 (wherein the primary cell of the hematopoietic system or hematopoietic stem cell is a CD34 positive cell or a precursor thereof) would be improperly excluded from the genus.

The procedure for handling applications that include generic claims is set forth in 37 CFR §1.146. This rule provides that "[i]n the first action on an application containing a generic claim to a generic invention (genus) and claims to more than one patentably distinct species embraced thereby, the examiner may require the applicant in the reply to that action to elect a species of his or her invention to which his or her claim will be restricted if no claim to the genus is found to be allowable." (emphasis added)

As stated in MPEP § 809.02(a), "[u]pon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141." Thus, where generic claims are present, an applicant can be required to elect a species for initial examination, but the generic claims are still subject to examination to determine whether such generic claims are allowable (MPEP §809.02(a), 8th ed., rev. 2, May 2004, pg 800-49).

In the instant restriction requirement, this required procedure is not being followed. Claims 1, 34 and 88 are proper generic claims within the requirements set forth in 37 CFR § 1.141. Claim 1 satisfies the definition of a generic claim as set forth in MPEP §806.04(d), in that it includes limitations that are not present in all claims that depend from it. Therefore, an election of species requirement is permissible, but a restriction requirement is not. (MPEP §806.04(d), 8th ed., rev. 2, pg 800-41).

Moreover, because this "patentably distinct" species/restriction requirement splits claim 1 into multiple groups, the restriction requirement is improper as a matter of law. The courts have long held that the section of the patent statute that authorizes restriction practice, *i.e.*, 35 U.S.C. 121,

provides no legal authority for not examining a broad generic claim. See, In re Weber, 198 USPQ 328, 331 (CCPA 1978); In re Haas, 179 USPQ 623, 624-625 (*In re Haas I*) (CCPA 1973) and In re Haas 198 USPQ 334-337 (In re Haas II) (CCPA 1978). As stated in In re Weber:

> "The discretionary power to limit one applicant to one invention is no excuse at all for refusing to examine a broad generic claim—no matter how broad, which means no matter how many independently patentable inventions may fall within it." 198 USPQ 328 at 334. (emphasis added)

In a case such as the instant case, where a claim is generic, a restriction requirement is tantamount to a rejection of the claim. The CCPA made this point very clear in In re Haas I:

> "We find that the action taken by the examiner did in fact amount to a rejection. . . . Those claims were withdrawn from consideration not only in this application but prospectively in any subsequent application because of their content. In effect there had been a denial of patentability of the claims. Presumably only by dividing the subject matter into separate, and thus different, claims in plural applications could an examination of the patentability of their subject matter be obtained." 179 USPQ at 625.

If the instant restriction requirement is allowed to stand, Applicants will not be accorded "the basic right of the applicant to claim his invention as he chooses." In re Weber, 198 USPQ at 331. In In re Weber, the CCPA stated that "[a]s a general proposition, an applicant has a right to have *each* claim examined on the merits" (198 USPQ at 331, emphasis in original). The Court went on to state that:

> "If . . . a single claim is required to be divided up and presented in different applications, that claim would never be considered on its merits. The totality of the resulting fragmentary claims would not necessarily be the equivalent of the original claim. Further, since the subgenera would be defined by the examiner rather than by the applicant, it is not inconceivable that a number of the fragments would not be described in the specification." 198 USPQ at 331.

Since the decisions in In re Weber, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and *In re Haas,* 580 F.2d 461, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention. MPEP §803.02, 8th ed., rev. 2, May 2004, pg 800-4. Even if Applicants were to file multiple divisional applications in addition to the instant application to obtain coverage for each of the alleged patentably distinct species, we would not have the opportunity to have our broader

generic claim examined, i.e., we would not have the opportunity to have that which Applicants regard as their invention examined. The claims of the various divisional applications would be limited to the particular species set forth in the respective groups. For example, one seeking to avoid infringement could simply choose a cell surface binding molecule that is not specifically disclosed in the application. In effect, the restriction requirement is reading into Applicants' independent claims limitations that are not present in the claims as filed. The full scope of claims 1 and 34, as filed and pending, for example, would never be considered under the current species restriction requirement. Only the dependent claims which are set forth in the respective groups would be examined.

Applicants therefore respectfully request that the instant restriction requirement with respect to "patentably distinct species" be withdrawn and treated as though it were a species election under the procedure set forth in MPEP 809.02(a). Applicants request that, upon allowance of a generic claim, the remainder of the species be included as permitted by 37 C.F.R. § 1.141(a).

Pursuant to 37 C.F.R. § 1.144, Applicants reserve the right to petition for review of the restriction requirement at any time prior to appeal. Applicants also submit that because the instant restriction requirement is tantamount to a rejection of the generic independent claims (claim 1, claim 34, and new claim 88) the restriction requirement is appealable to the Board of Patent Appeals and Interferences. In re Haas I. If the instant restriction requirement is allowed to stand, Applicants will not be accorded "the basic right of the applicant to claim his invention as he chooses." In re Weber. It is improper for the Office to refuse to examine that which Applicants regard as their invention. MPEP §803.02, 8th ed., rev. 2, May 2004, pg 800-4.

Accordingly, Applicants respectfully request reconsideration of the restriction requirement and request that the restriction requirement with respect to the "patentably distinct species," as discussed above, be withdrawn and treated as though it were a species election under the procedure set forth in MPEP 809.02(a).

CONCLUSION

Applicants have respectfully requested reconsideration of the restriction requirement; in particular, they have requested that the restriction requirement with respect to the "patentably distinct species," as discussed above, be withdrawn and treated as though it were a species election under the procedure set forth in MPEP 809.02(a).

Applicants have set forth distinct and specific errors in the restriction requirement and reasons for the Patent Office to reconsider and withdraw the restriction requirement. Accordingly, Applicants have preserved their right to petition the restriction to the Group Director under 37 CFR §1.144; see also MPEP §818.03(c); pg 800-60, 8th Edition, rev. 2, May 2004. Applicants may defer submission of the petition (which can be deferred until allowance of the claims).

It is believed that the all claims pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

In the unlikely event that the transmittal form is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing 397272000401. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

As noted above, Applicants have requested a telephone conference with the undersigned representative to expedite prosecution of this application. After the Examiner has reviewed the instant response and amendment, please telephone the undersigned at (858) 720-5133.

Dated: December 20, 2005

Respectfully submitted,

By _____

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